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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,313	03/07/2005	Michael Bardroff	F2842 US S3 (C018016/0180	1924

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,313	BARDROFF ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007 and 25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-16,22 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-16,22 and 28-30* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-9,11-16,22 and 28-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/20/04, 8/6/07, 11/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' elections with traverse of Group I, claims 1-16, 22 and 28-30, and of species B) MSR-7 antibody, in the reply filed on 27 July 2007 are acknowledged. Because applicants did not distinctly and specifically point out the supposed errors in the restriction and election of species requirements, the elections have been treated as elections without traverse (MPEP § 818.03(a)).

Response to Amendment

Claims 10, 17-21, 23-27 and 31-40 have been canceled as requested in the amendment filed on 25 October 2007. Following the amendment, claims 1-9, 11-16, 22, and 28-30 are pending in the instant application.

Claims 1-9, 11-16, 22, and 28-30 are under examination in the instant office action.

Sequence Rules Requirement

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). Therefore, the application must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Therefore, the application must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). However the

instant application is not in compliance with the sequence rules, particularly 37 C.F.R. § 1.821(d), which requires that reference be made to a particular sequence identifier (SEQ ID NO:) in the specification and claims at each disclosure of a sequence encompassed by the definitions set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). The instant claim 3 and supporting sections of the specification contain sequences, which are not properly identified.

In case these sequences are new, Applicants must provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification wherever a reference is made to that sequence. For rules interpretation Applicants may call (703) 308-1123. See M.P.E.P. 2420-2435. Applicants are advised to review the entire text of the instant specification for compliance with sequence rules.

Information Disclosure Statements

Signed and initialed copies of the IDS papers filed on 20 August 2004, 06 August 2007 and 13 November 2007 are enclosed in this action.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies or fragments thereof that comprise 6 CDRs, three from the VH domain and three from the VL domain, wherein the antibodies and fragments thereof bind the same antigen as claimed, does not reasonably provide enablement for an antibody and fragments thereof that do not contain a full set of 6 CDRs from the VH and the VL domains as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative

skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

Claims 4-6 are broadly drawn to antibodies or fragments thereof, comprising only a VH and/or a VL domain that do not contain a full set of 6 CDRs from the VH and the VL domains.

The specification discloses only antibodies that contain both a VH and a VL chain with no less than 6 CDRs, 3 from the VH chain and 3 from the VL chain that bind to antigen (see Table 1, pp.64-68). The specification does not enable antibodies and fragments thereof, which do not contain 6 CDRs and bind antigen.

It is well established in the art that the formation of an intact antigen-binding site of all antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope (Paul, Fundamental Immunology, (textbook), 1993, pp. 292-295, under the heading "Fv Structure and Diversity in Three Dimensions"). The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites (Paul, page 293, first

column, lines 3-8 and line 31 to column 2, line 9 and lines 27-30). Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA 1982 Vol. 79: page 1979). The Rudikoff et al. reference teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that the antibodies and fragments thereof as defined by the claims, which may contain less than the full complement of CDRs from the heavy and light chain variable regions have the required binding function. Applicants have provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability of producing an antibody and fragments thereof containing fewer than 6 CDRs, resulting in an antibody that retains the antigen specificity currently claimed. However, the claim language also reads on small amino acid sequences, which are incomplete regions of the variable region of the antibody. One of skill in the art would neither expect nor predict the appropriate functioning of the antibodies as broadly as is claimed. Therefore, in view of the lack of guidance in the specification and in view of the discussion above, undue experimentation would indeed be required to make and use the invention commensurate with the scope of the claims.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it

The invention appears to employ novel biological materials, specifically the MSR-3, MSR-7 and MSR-8 antibodies. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. It appears that Applicants have not deposited the biological materials, and a deposit at a recognized depository may be made for enablement purposes. If a deposit has been made under the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, and that the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicants' attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information; however, Applicants are cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicants are advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection
10801 University Boulevard
Manassas, VA 20110-2209

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims depend from canceled claims, i.e. claims 17 and 18 and 27, respectfully. Thus, the metes and bounds of claims 22 and 28 cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 8, 9, 15, 16, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,955,317 to Suzuki et al (citation A3 on the IDS dated 13 November 2007.

The claims are directed to an antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/A β4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof

and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof.

The Suzuki et al. patent teaches a monoclonal antibody that specifically recognizes two regions of the β-amyloid (i.e., β-A4) peptide, wherein the two regions are the amino acid sequences of SEQ ID NO: 7 and SEQ ID NO: 10 (see claim 1, for example). The Suzuki et al. patent's SEQ ID NO: 7 is the amino acid sequence DAEFRHDSGYEVHHQKLVFFAEDVGSNK, which comprises both the instant SEQ ID NO: 1 and the instant SEQ ID NO: 2 (see cols. 47-48), and the Suzuki et al. patent's SEQ ID NO: 10 is the amino acid sequence DAEFRHDSGYEVHHQK, which comprises the instant SEQ ID NO: 1 and fragment of the instant SEQ ID NO: 2 (see cols. 49-50). Thus, the limitations of claims 1 are taught by the Suzuki et al. patent. Given that the antibody of the Suzuki et al. patent specifically recognizes the two regions claimed, the antibody would recognize at least two consecutive amino acids within the two regions, thus meeting the limitations of claim 2. Also, absent evidence to the contrary, the antibody would bind to at least one of the regions of SEQ ID NO: 1 and to at least one of the regions of SEQ ID NO: 2 recited by claim 3, thus meeting the limitations of claim 3. The patent teaches that the antibodies of the invention can be full-length, a F(ab)-fragment and a $F(ab)_2$-fragment (col.18, lines 10 and 11), thus meeting the limitations of claim 8. Moreover, given that the two regions of the β-A4 peptide are separated by at least 1 amino acid, the regions form a discontinuous or conformational epitope, thus meeting the limitations of claim 9. The patent also teaches pharmaceutical compositions (abstract), thus meeting the limitations of claims 15, 16, 29 and 30. It is

noted that claim 29 is a product-by-process claim. Given that the patent teaches the product itself, said claim is anticipated. A product made by any other process renders a product-by-process claim unpatentable. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985).

Since the patent teaches all the elements of the claims, claims 1-3, 8, 9, 15, 16, 29 and 30 are anticipated by U.S. Patent No. 5,955,317 to Suzuki et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,955,317 to Suzuki et al (citation A3 on the IDS dated 13 November 2007) in view of Knappik et al. (citation C3 on the IDS dated 20 August 2004).

The claims are drawn to a nucleic acid, vector and host cell that encode the antibody molecule capable of specifically recognizing two regions of the β-A4 peptide/A β4, wherein the first region comprises the amino acid sequence AEFRHDSGY as shown in SEQ ID NO: 1 or a fragment thereof and wherein the second region comprises the amino acid sequence VHHQKLVFFAEDVG as shown in SEQ ID NO: 2 or a fragment thereof.

The Suzuki et al. patent teaches as set forth above, but does not teach encoding nucleic acids, vectors or host cells. However, determining the amino acid sequence of the antibody and then the encoding nucleic acid is standard and known in the art as evidenced by the Knappik et al. reference (p.58, col.1). The Knappik et al. reference

teaches nucleic acid-vector-host cell expression and production of antibodies (p.58), as in the instant claims 11-14.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by combining the antibody of the Suzuki et al. patent with the disclosure of the Knappik et al. reference. The skilled artisan would have been motivated to make these modifications to express the antibody recombinantly because of the advantages of doing so, as taught by the Knappik et al. reference (entire document, e.g., p.58, col.1). The person of ordinary skill in the art would have had a reasonable expectation of success because both references teach that the products and methods would work (entire documents).

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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22 January 2008

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